REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

Status

As is correctly reflected in the Office Action Summary, Claims 1-13 are pending. Claims 1-4, 11, and 12 stand rejected. Claims 5-10 and 13 are objected to.

Summary of Amendments

By the foregoing amendments, Claims 1-13 have been amended to correct minor, typographical, and stylistic issues. Specifically, Claims 4-7, 10, and 13 were amended to remove the phrase "one of the preceding claims" and to create dependency upon independent claim 1. Support for these amendments may be found in original Claims 4-7, 10, and 13. Accordingly, no new matter has been added.

Also by the foregoing amendments, Claim 2 was amended to remove the phrase "preferably between 200 and 600 µm." New Claim 14 was added to cover this subject matter. Accordingly, no new matter has been added by the addition of Claim 14.

Finally by the foregoing amendments, Claim 1 was amended to specify that the active principle is formed by direct compression of microgranules containing the active principle, and to specify that said active principle is attached a coating to

neutral microgranules and is not coated with an agent intended to modify its release or to mask its taste. Support for these amendments can be found at, *inter alia*, Page 6, Lines 1-6, and Page 10, Line 38 to Page 11, Line 7, of the Specification. Accordingly, no new matter has been added.

Rejections Under 35 U.S.C. § 102 over Koyama

Claims 1, 2, 4, and 11 were rejected under 35 U.S.C. § 102(b) as purportedly anticipated by EP 0 361 874 to Koyama *et al.* ("Koyama"). *See Official Action, Page 2.* This rejection is respectfully traversed.

To anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). Applicants assert that Koyama fails to contain all elements of Claims 1, 2, 4, and 11. Claims 1, 2, 4, and 11, as amended, are directed to a tablet comprising a low dose of active principle. In this tablet, the active principle is attached as a coating to neutral microgranules. The tablet is obtained by *direct compression* of these *neutral microgranules* which carry the active principle. If a thin layer of active principle is adsorbed onto the neutral microgranules, as is the case in a low-dose tablet, then the tableting properties of the granules are not modified and they can be directly compressed into tablets. In the context of Applicants' invention, the expression "neutral microgranules" means spherical granules comprising sucrose and starch. *See, e.g., Page 10, Lines 31-37 of the Specification.*

Contrarily, Koyama is directed to the preparation of granules containing an active principle by using a centrifugal fluidized-bed coating granulator ("CF

granulator"). Koyama admits that CF granulators may damage the spherical granules at their initial stages. *See, e.g., Koyama Page 2, Lines 28-36.* Koyama indicates that spraying seed granules with a dispersion of low-substituted hydroxypropyl cellulose (L-HPC) can yield to spherical granules having enhanced granule strength and improved disintegration properties. *See, e.g., Koyama Page 2, Lines 37-46.*

Koyama explains the preparation of granules having a neutral core, on which a solution containing L-HPC is sprayed, an active principle, and other excipients. S*ee Koyama Examples 3 and 4.* The granules may be covered with an enteric coating. S*ee Koyama Examples 1, 2 and 5.* The granules may be compressed into tablets. Example 2 is the only example of Koyama disclosing the preparation of a tablet. In Example 2, the tablets are formed by compression of a mixture comprising 420 g of *enteric-coated* granules of Serrapeptase sprayed onto neutral cores, 270 g of aluminum hydroxide sodium hydrogeno-carbonate coprecipitate, 580 g cystalline cellulose, 150 g magnesium strearate, and 1440 g of granules for tablet compression (prepared by granulating a mixture of various ingredients, yet *not* by spraying a coating onto neutral cores).

Applicants maintain that because Koyama does not form tablets via *direct compression*, as required by Claims 1, 2, 4, and 11, Koyama does not anticipate these claims.

Rejections Under 35 U.S.C. § 103(a) over Koyama in view of Giannini

Claims 1-4, 11, and 12 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Koyama in view of U.S. Patent No. 4,925,674 to Giannini *et al.* ("Giannini"). *See Official Action, Pages 2-3.* This rejection is respectfully traversed.

When applying 35 U.S.C. § 103, four tenets of patent law must be adhered to: (1) the claimed invention must be considered as a whole, (2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, (3) the references must be viewed without the benefit of impermissible hindsight vision, and (4) a reasonable expectation of success is the standard with which obviousness is determined. *See MPEP § 2141*, citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 (Fed. Cir. 1986). To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See MPEP § 2142.*

Moreover, mere identification of each claimed element in the prior art is not sufficient to negate patentability. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Instead, there "must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the filed of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 536 (Fed. Cir. 1998). Otherwise, sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. *Rouffet*, 149 F.3d at 1357.

As indicated above, Koyama fails to disclose forming tablets via direct compression. Giannini does not cure this deficiency. Giannini pertains to amoxicillin microencapsulated granules with an active density greater than about 0.200 g/ml, or a potency which is about 650 mg/g to about 750 mg/g. *See, e.g., Giannini, Column 6, Lines 47-48.* In Giannini, the active coating is applied onto inert seeds (*see Column 5, Line 19*) and the granules preferably have a taste mask coating. *See, e.g., Giannini, Column 3, Lines 42-43.* The granules afford accurate delivery of an appropriate does by weight of amoxicillin, thereby avoiding adverse effects due to overdose. *See Giannini, Column 3, Lines 14-25.*

Neither Koyama nor Giannini teach or suggest that neutral microgranules may be *directly compressed* into tablets. Because Koyama in view of Giannini fail to teach or suggest the limitation in Applicants' claims that the active principle is formed by direct compression of microgranules containing the active principle, a *prima facie* case of obviousness has not been made out. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection of Claims 1-4, 11, and 12 over Koyama in view of Giannini.

CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any remaining questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (703) 838-6526 so that prosecution of the application may be expedited.

Respectfully submitted,
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